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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/672,794	09/25/2003	Teodorica L. Bugawan	022101-002610US	1789

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EXAMINER
SWITZER, JULIET CAROLINE

ART UNIT	PAPER NUMBER
1634	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,794	BUGAWAN ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-85* is/are pending in the application.

4a) Of the above claim(s) *1-21,37-82,84 and 85* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-36 and 83* is/are rejected.

7)☒ Claim(s) *34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/04; 6/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II, further electing species SEQ ID NO: 24 in the reply filed on 12/21/06 is acknowledged.

2. Claims 1-21, 37-82, and 84-85 withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/21/06.

3. It is noted that instant claim 83 refers to non-elected claim 77. Prior to any eventual allowance, claim 83 will be required to be amended to be in independent form.

Claim Objections

4. Claim 34 is objected to because it refers to "polynucleotide sequences listed in Table 9." MPEP 2173.05(s) states "Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table 'is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplicating a drawing or table into the claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience.'" In this case, the nucleic acid sequences in Table 9 can be referred to by proper SEQ ID NO. Correction is required.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 22, 25, 27-32, 36 and 83 are rejected under 35 U.S.C. 102(a) as being anticipated by Noble et al. (Human Immunology, Vol. 63, pages 657-664, August 2002; cited in IDS).

Noble et al. teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele indicates the individual's decreased risk for type I diabetes (p. 658). Namely, Noble et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (p. 658). They further teach that six alleles revealed significant or nearly significant deviations from values expected under the null hypothesis, in particular teaching that the A*1101 allele is more frequent in the control population than the patients with diabetes (Table 1), thus they teach that this allele is a "protective allele."

Regarding claims 25 and 27-30, the alleles are amplified and detected using PCR. After PCR the nucleic acid sample comprises DNA. Regarding claim 31, hybridization to allele specific oligonucleotides is a means of sequencing insofar is it provides data about the sequence of the hybridized molecules. Regarding claim 32, the sequence specific oligonucleotide probe method, as suggested by the title of the method, a method where an allele is detected by contacting a nucleic acid sample with one or more polynucleotides that hybridize to one or more polymorphisms associated with said alleles and detecting hybridization. Regarding claim 36, for each individual two alleles are detected since all individuals were genotyped and all individuals carry two copies of the gene. Regarding claim 83, Noble et al. teach that the sequence specific probes were immobilized since refer to reference numbered 19 and the title of

this reference includes the teaching that the probes are immobilized (p. 658 and 664). Thus, the set of immobilized sequence specific probes is an array for determining an individual's risk, and Noble et al. contact nucleic acid samples with the array and the presence of the alleles is correlated with diabetes risk as taught by Noble et al.

7. Claims 22, 23, 24, 25, 27-33, 36, and 83 are rejected under 35 U.S.C. 102(a) as being anticipated by Bugawan et al. (Tissue Antigens (June 2002) 59:452-469; Cited in IDS).

Bugawan et al. teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele indicates the individual's decreased risk for type I diabetes (p. 453-454). Namely, Bugawan et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (p. 454). They further teach that alleles revealed significant or nearly significant deviations from values expected under the null hypothesis, in particular teaching that the A*1101 allele is more frequent in the control population than the patients with diabetes (p. 467), thus they teach that this allele is a "protective allele." Regarding claims 23 and 24, the individuals typed are Asian, namely Filipino (p. 453).

Regarding claim 25 genomic DNA is isolated (p. 453) and regarding 27-30, the alleles are amplified and detected using PCR. Regarding claim 31, hybridization to allele specific oligonucleotides is a means of sequencing insofar is it provides data about the sequence of the hybridized molecules. Regarding claim 32, the sequence specific oligonucleotide probe method, as suggested by the title of the method, a method where an allele is detected by contacting a nucleic acid sample with one or more polynucleotides that hybridize to one or more polymorphisms associated with said alleles and detecting hybridization. Regarding claim 33,

Bugawan et al. amplified exons 2 and 3 from the gene, so the probes inherently had to hybridize to this region for detection. Regarding claim Regarding claim 36, for each individual two alleles are detected since all individuals were genotyped and all individuals carry two copies of the gene. Regarding claim 83, Bugawan et al. teach that the sequence specific probes were immobilized since refer to reference numbered 19 and the title of this reference includes the teaching that the probes are immobilized (p. 454). Thus, the set of immobilized sequence specific probes is an array for determining an individual's risk, and Bugawan et al. contact nucleic acid samples with the array and the presence of the alleles is correlated with diabetes risk as taught by Bugawan et al.

8. Claims 22, 23, 24, 25, 27-32, and 36 are rejected under 35 U.S.C. 102(b) as being anticipated by Bugawan et al. (European Journal of Immunogenetics, Volume 28, Issue 2, page 289, abstract numbered 183, April 2001; cited in IDS).

Bugawan et al. teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele indicates the individual's decreased risk for type I diabetes. Namely, Bugawan et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (referred to as PCR/SSOP). They further teach that HLA-A 2407 allele frequency was decreased in patient populations, thus they teach that this allele is a "protective allele." Regarding claims 23 and 24, the individuals typed are Asian, namely Filipino.

Regarding claim 25, after PCR DNA is in the sample, and regarding 27-30, the alleles are amplified and detected using PCR. Regarding claim 31, hybridization to allele specific oligonucleotides is a means of sequencing insofar is it provides data about the sequence of the

hybridized molecules. Regarding claim 32, the sequence specific oligonucleotide probe method, as suggested by the title of the method, a method where an allele is detected by contacting a nucleic acid sample with one or more polynucleotides that hybridize to one or more polymorphisms associated with said alleles and detecting hybridization. Regarding claim Regarding claim 36, for each individual two alleles are detected since all individuals were genotyped and all individuals carry two copies of the gene.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 33-35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Noble et al. in view of Bugawan et al. (Tissue Antigens, 1994: 44:137-147).

Noble et al. teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele

indicates the individual's decreased risk for type I diabetes (p. 658). Namely, Noble et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (p. 658). They further teach that six alleles revealed significant or nearly significant deviations from values expected under the null hypothesis, in particular teaching that the A*1101 allele is more frequent in the control population than the patients with diabetes (Table 1), thus they teach that this allele is a "protective allele." The sequence specific oligonucleotide probe method, as suggested by the title of the method, a method where an allele is detected by contacting a nucleic acid sample with one or more polynucleotides that hybridize to one or more polymorphisms associated with said alleles and detecting hybridization.

Noble et al. do not teach that the sequence specific oligonucleotides are complementary to a sequence found in exon 2 or exon 3 of a protective HLA-A allele. Noble et al. do teach that they were following the methods of Bugawan et al. (1994).

Bugawan et al. teach a method for typing HLA-A locus which uses PCR amplification and immobilized oligonucleotide probes. The probes taught by Bugawan et al. are specific to exon 2 and 3 of HLA-A alleles, including probes in both exons which hybridize to protective allele A*1101 (Table 1 and Figure 4), including instant SEQ ID NO: 24, which is probe DB436 taught by Bugawan et al.

Thus, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by Noble et al. so as to have used the probes and methods for genotyping taught by Bugawan et al. One would have been motivated to have modified the methods taught by Noble et al. by Noble et al.'s express

suggestion to look to Bugawan et al. for genotyping methods, and by Bugawan et al.'s success in genotyping the complicated HLA-A region using PCR and immobilized oligonucleotide probes.

12. Claim 26 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bugawan et al. (2001).

Bugawan et al. (2001) teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele indicates the individual's decreased risk for type I diabetes. Namely, Bugawan et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (referred to as PCR/SSOP). They further teach that HLA-A 2407 allele frequency was decreased in patient populations, thus they teach that this allele is a "protective allele."

Bugawan et al. (2001) do not teach that the nucleic acid sample comprises RNA. However, at the time the invention was made, it was routine in the prior art to isolate DNA and RNA from patient samples in order to be used in genotyping assays, as were direct hybridization methods which required no prior nucleic acid extraction. Thus, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by Bugawan et al. (2001) so as to have isolated total nucleic acids from the patient samples for genotyping or to have used a rapid prep method which did not require nucleic acid extraction. In either case, the tested sample would have contained DNA and RNA. One would have been so motivated in order to have provided additional means for carrying out the genotyping methods taught by Bugawan et al. In the absence of a secondary consideration, therefore, the claimed invention is prima facie obvious.

13. Claims 33, 34, and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bugawan et al. (2001) in view of Bugawan et al. (1994).

Bugawan et al. (2001) teach a method comprising detecting the presence of a protective class I HLA-A allele in a nucleic acid sample of an individual wherein the presence of said allele indicates the individual's decreased risk for type I diabetes. Namely, Bugawan et al. teach molecular HLA typing using a polymerase chain reaction, sequence specific oligonucleotide probe method (referred to as PCR/SSOP). They further teach that HLA-A 2407 allele frequency was decreased in patient populations, thus they teach that this allele is a "protective allele."

Bugawan et al. (2001) do not teach that the sequence specific oligonucleotides are complementary to a sequence found in exon 2 or exon 3 of a protective HLA-A allele, nor do they teach a method wherein one or more of the polynucleotides comprise SEQ ID NO: 24 or any other nucleic acid in Table 9. Regarding claim 83, Bugawan et al. do not teach that their probes are on an array. Bugawan et al. also do not teach a method wherein the nucleic acid sample is RNA.

Bugawan et al. (1994) teach a method for typing HLA-A locus which uses PCR amplification and immobilized oligonucleotide probes. The probes taught by Bugawan et al. are specific to exon 2 and 3 of HLA-A alleles, including probes in both exons which hybridize to protective allele A*1101 (Table 1 and Figure 4), including instant SEQ ID NO: 24, which is probe DB436 taught by Bugawan et al. Regarding claim 83, the immobilized probe assay taught by Bugawan et al. is an array for comprising one or more polynucleotides that each hybridize under stringent hybridization conditions to a nucleic acid sequence in a type I diabetes-class I HLA-A allele.

Thus, at the time the invention was made, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods taught by Bugawan et al. (2001) so as to have used the probes and methods for genotyping taught by Bugawan et al. (1994). One would have been motivated to have modified the methods taught by Bugawan et al. (2001) by the success of Bugawan et al. (1994) in genotyping the complicated HLA-A region using PCR and immobilized oligonucleotide probes, and because Bugawan et al. (1994) teach that their method "allows individual samples to be analyzed with a single hybridization with a membrane..." and that "the availability of all the typing information on a single strip minimizes the potential for errors in genotype interpretation (p. 146)."

14. Claims 22, 25-36, and 83 are rejected under 35 U.S.C. 103(a) as being unpatentable over Slater et al. (J. Clin. Lab. Immunol (1980)4, 91-94) in view of GenBank Record Accession AF030897, dated 25 November 1997 and Bugawan et al. (1994).

Slater et al. teach a method which comprises the steps of detecting the presence of a protective class I HLA-A allele in a sample of an individual, wherein the presence of said allele indicates an individual's decreased risk for type 1 diabetes. Namely, Slater et al. teach analyzing the frequency of HLA-A types in a set of type 1 diabetes patients and healthy controls (p. 91), and teach that the presence of HLA-A11 confers a statistically significant protection against disease development in these patients (p. 91 and 92).

Slater et al. do not teach a method wherein the HLA-A allele is determined in a nucleic acid sample.

The GenBank record provides the nucleic acid sequence of A11 allele A*1101.

Bugawan et al. teach a method for typing the HLA-A locus using PCR amplification and immobilized oligonucleotide probes. Regarding claim 25, after PCR DNA is in the sample, and regarding 27-30, the alleles are amplified and detected using PCR. Regarding claim 31, hybridization to allele specific oligonucleotides is a means of sequencing insofar is it provides data about the sequence of the hybridized molecules. Regarding claim 32, the sequence specific oligonucleotide probe method, as suggested by the title of the method, a method where an allele is detected by contacting a nucleic acid sample with one or more polynucleotides that hybridize to one or more polymorphisms associated with said alleles and detecting hybridization. Regarding claim 36, for each individual two alleles are detected since all individuals were genotyped and all individuals carry two copies of the gene. The probes taught by Bugawan et al. are specific to exon 2 and 3 of HLA-A alleles, including probes in both exons which hybridize to protective allele A*1101 (Table 1 and Figure 4), including instant SEQ ID NO: 24, which is probe DB436 taught by Bugawan et al. Regarding claim 83, the immobilized probe assay taught by Bugawan et al. is an array for comprising one or more polynucleotides that each hybridize under stringent hybridization conditions to a nucleic acid sequence in a type I diabetes-class I HLA-A allele.

Bugawan et al. teach that the serology to detect class I types requires large amounts of sera and lymphocytes, while they exemplify that their method can be performed on extracted nucleic acids (p. 144 and throughout). They further that their disclosed method is simple, rapid to perform, produces detectable signals in minutes and should prove valuable for tissue typing (p. 138). Thus, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have modified the methods taught by Slater et al. so as to have

detected HLA-A alleles via the detection of nucleic acids instead of using detection by serology. One would have been motivated to modify the teachings of Slater et al. by the express teachings of Bugawan et al. as to the advantages of nucleic acid detection over serology, and also by the teaching of the GenBank record which expressly provides that A*1101 is an A11 allele. Thus, in view of the teachings of the prior art, the claimed invention is prima facie obvious.

Claim Rejections - 35 USC § 112

15. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 22-34, 36 and 83 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for method for detecting an individual's decreased risk for type 1 diabetes by detecting the presence of the A*1101 allele of class I HLA-A, does not reasonably provide enablement for methods which rely on the detection of any other "protective allele" within the class I HLA-A region. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Scope of the Claims

The claims are inclusive of the detection of the presence of any possible "protective class I HLA-A allele." The specification defines such an allele as any allele that has a negative association with the disease (¶0048). There are hundreds of different possible HLA-A alleles

that can be identified by nucleic acid genotyping. The claims encompass the detection of only those that are "protective."

Teachings in the specification

The specification teaches genotyping of ninety patients and ninety-four controls (Example 1 beginning on p. 29), and analysis of the frequencies of HLA-A alleles identified (p. 32). The specification teaches that HLA-A*1101 was negatively associated with type 1 diabetes, and thus is a protective allele (p. 33). This is the only protective allele identified. There is no guidance in the specification as to what common structural features would be shared by all protective alleles.

State of the art and level of unpredictability

The prior art of Bugawan et al. (2001) and the instant specification both teach that A*2407 is decreased in Filipino type 1 diabetes patients (instant specification ¶00145). Insofar as this disclosure is sufficient to enable the claims, the claims are also enabled for the practice of the claimed method for this allele. However, showing of a statistically significant relationship is given to support this assertion in either the reference or the instant specification.

There are hundreds of HLA-A alleles in humans. At the time the invention was made it was a priori highly unpredictable which of these alleles might be protective relative to diabetes type 1. It remains highly unpredictable. This unpredictability is exemplified in the instant specification which teaches that the A*24 group was reported to be increased among Caucasians, yet in the population tested in this specification, the A*24 alleles were statistically heterogeneous for type 1 diabetes (¶0143). Thus, the only means for determining whether a particular allele is protective or not is to undertake population based studies where the allele is identified and

attempts to observe statistically significant associations are made. Further, Noble et al. (2002; IDS) teach that simply comparing frequencies for a given allele in patients and controls may misrepresent true susceptibility for that allele, pointing out that after correction for linkage disequilibrium and an allele that appeared to be predisposing was seen as protecting after correction (p. 663). Thus, associating HLA-A alleles with the diabetes phenotype is highly unpredictable.

Quantity of Experimentation

The specification demonstrates the type of experimentation that would have to be undertaken in order to identify additional "protective alleles" of the HLA-A locus. Such experimentation would have to be undertaken in hundreds of thousands of individuals in order to identify for each HLA-A allele enough subjects who carry the alleles in diabetic and healthy controls to allow the analysis of the alleles to determine if they are protective or not. While many HLA-A alleles had been identified in the prior art, there is no a priori way to predict if a particular allele is protective, or not, and so, to practice the claims commensurate in scope with their broad scope, which encompasses detecting any possible protective allele, an enormous amount of experimentation would be required.

Conclusion

Thus, considering these factors, especially the breadth of the claims, the unpredictability of the technology, and the limited guidance in the specification, it is concluded that it would require undue experimentation to make and use the claimed invention commensurate in scope with the claims.

17. Claims 22-34, 36 and 83 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn the detection of the presence of any "protective class I HLA-A allele." The practice of the invention encompasses the detection of any class I HLA-A allele that is "protective" relative to type 1 diabetes, wherein the presence of the allele indicates an individual's decreased risk for type 1 diabetes. The practice of the invention encompasses the detection of HLA-A alleles described in the prior art but not yet identified as "protective" and of HLA-A alleles not yet identified which may be protective. The specification identifies a single allele as protective, namely HLA-A*1101.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2b 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed". Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. In *The Regents of the University of California v. Eli Lilly* (43 USPQ2b 1398-1412), the court held that a generic statement which defines a genus of nucleic acids by only their functional activity does not provide an adequate written description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court

states that "An adequate written description of a DNA...' required a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

With respect the instant claims which encompass the identification of unidentified polymorphic sequences, no common structural attributes identify the members of the genus. The current claims encompass detecting "protective" alleles which may be any of a large genus of known and unidentified HLA-A alleles. The genus of "protective" alleles is represented in the specification by only the particularly named allele for which data is provided. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, "protective class I HLA-A allele" alone is insufficient to describe the genus. There is no description of how to select "protective" alleles from the large genus (hundreds) of possible HLA-A alleles. The general knowledge in the art concerning variants does not provide any indication of how the structure of one allele is representative of unknown alleles. The nature of alleles is such that they are variant structures, and in the present state of the art the structure of one does not provide guidance to the structure or function of others. The common attributes are not described. The specification provides no correlation between structure of polymorphisms and the function of such polymorphisms. The polymorphisms shown are not representative of the genus of any polymorphism. One of skill in the art would conclude that applicant was not in possession of the claimed genus because a description of only one member of this genus is not representative of the variants of the genus and is insufficient to support the claim.

Accordingly, Applicants have not adequately disclosed the relevant identifying characteristics of a representative number of species within the claimed genus.

Conclusion

18. No claim is allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday, Tuesday, or Thursday, from 9:00 AM until 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached by calling (571) 272-0735.

The fax phone numbers for the organization where this application or proceeding is assigned are (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the

problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Primary Examiner
Art Unit 1634

March 16, 2007